polyatomic ions of the discovery from polyatomic ions of the prior art applicant has depended upon claims with a requirement that all ions have more than some specified minimum number of charges. The problem then becomes to set a lower limit on the number of charges per ion above which no ions have ever been encountered in the prior art. If one sets that limit too low there is a danger that some obscure paper might show up reporting the previous production of a few polyatomic ions having that many charges. If the minimum number is set too high, there may occur a window of opportunity in which investigators might use electrospray ionization to produce multiply charged ions that did not infringe the patent claims but were useful for some important and valuable purpose.

Applicant has recently realized that there is another and not previously appreciated feature of the multiply charged ions of the subject discovery that further distinguishes them from ions of the prior art. That feature is clearly evident in the mass spectra shown in Figures 2A-2F of the specification and is characteristic of all electrospray ions of relatively large polyatomic molecules. It is that beginning with the peak at the lowest value of m/z (i.e. the highest number of charges per ion), the amplitudes of successive peaks increase with increasing m/z (i.e. decreasing number of charges per ion) up to some maximum (critical) value and then decrease with further increases of m/z, (i.e. further decreases in the number of charges per ion) finally becoming too small to be seen above the noise level. This rise and fall of peak amplitudes with increasing values of m/z indicates that the number of ions in a particular charge state first increases as the number of charges per ion in

that particular charge state decreases and then decreases as the number of charges per ion decreases beyond a critical value which depends upon the particular parent species. This rise and fall of ion abundance with decreasing ion charge state is a characteristic property of ions produced by electrospray ionization. This feature is absent in ions formed by other ionization methods such as laser desorption which generally show a monotonic increase in ion abundance with decreasing number of charges per ion so that singly charged ions are the most abundant. Ions produced by Thermospray ionization sometimes show vestiges of this behaviour but the maximum number of charges on such ions is generally much too small to support firm conclusions about a persistent trend over a wide range of charges states as shown in the panels of Figure 2.

New Claims 200-214, that applicant seeks to add, all provide for distinguishing the ions of the discovery from the ions of the prior art by the unique rise and full of ion abundance with increasing ion charge state which is a characteristic and distinctive feature of the ion populations claimed as a new composition of matter. Applicant earnestly hopes that the Examiner will grant the request to add these new claims to the application.

Respectfully Submitted,

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